



## Case Report

# Recognizing Granulomatosis with Polyangiitis in Bullous Purpura Presentations

**Manjushree Shanmugasundaram<sup>1\*</sup>, Rebekah Brown<sup>1</sup>, Meghana Koleti<sup>2</sup>, Anita C Mercado<sup>2</sup>**

<sup>1</sup>John Sealy School of Medicine, The University of Texas Medical Branch, Galveston, Texas, USA

<sup>2</sup>Department of Internal Medicine, The University of Texas Medical Branch, Galveston, Texas, USA

**\*Corresponding author:** Manjushree Shanmugasundaram, John Sealy School of Medicine, The University of Texas Medical Branch, Galveston, Texas, USA

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### Abstract

Granulomatosis with polyangiitis has a variable presentation making diagnosis difficult as it can be mistaken for IgA vasculitis which presents similarly. We report a case of granulomatosis with polyangiitis presenting with a bullous rash. Our patient was admitted for bullous purpura to the extremities, and reported symptoms of sinus infection, productive cough, and bilateral hearing loss which was first treated with Amoxicillin. Initially, drug-related IgA vasculitis was the leading diagnosis, given recent Amoxicillin exposure and bullous purpura findings. However, given the history of nasal involvement, hearing loss, and anti-proteinase 3 positivity, granulomatosis with polyangiitis was diagnosed per American College of Rheumatology criteria despite atypical bullous purpura. We highlight that the presence of a bullous rash does not exclude granulomatosis with polyangiitis. Timely workup with biopsy and anti-neutrophil cytoplasmic antibody positivity screening is imperative as early diagnosis of granulomatosis with polyangiitis can prevent long-term complications.

**Keywords:** Granulomatosis; Polyangiitis; Amoxicillin; Anti-neutrophil Cytoplasmic Antibodies; Immunosuppressive

### Introduction

Granulomatosis with polyangiitis (GPA) is a small to medium vessel pauci-immune vasculitis characterized by necrotizing granulomas affecting the upper respiratory tract (sinusitis, saddle nose deformity, otitis media, mastoiditis, hearing loss), lungs (nodules, alveolar hemorrhage), and kidneys (glomerulonephritis). Granulomatosis with polyangiitis often presents with lung (50% of cases) and kidney (10-20% of cases) involvement with upper respiratory insults such as sinusitis (90% of cases). Granulomatosis with polyangiitis can also present with dermatological involvement (50-60% of cases) including palpable purpura, and less frequently,

ulcers, papules, vesicles, and granulomas [1]. However, the presentation of granulomatosis with polyangiitis is variable making diagnosis less straightforward.

IgA vasculitis is the result of IgA-dominant immune complex deposition and clinically presents with cutaneous eruptions, abdominal pain, arthritis, and less commonly, glomerulonephritis. Cutaneous eruption is the most common presenting sign, including bullae, pustules, and hemorrhagic purpura. The cause of IgA vasculitis remains unknown, however, infections and drugs are well-described precipitating events. [2] Drug-induced IgA vasculitis is typically associated with warfarin, beta-lactam, fluoroquinolone, and macrolide use, while drug-induced ANCA vasculitis is related to hydralazine, propylthiouracil, or cocaine exposure. [3] Granulomatosis with polyangiitis can be mistaken

for IgA vasculitis, especially in the context of a drug-induced reaction. We report a case of granulomatosis with polyangiitis presenting with a bullous rash initially perceived as drug-induced IgA vasculitis.

### Case Presentation

An incarcerated female in her late 30s was admitted for necrotizing tonsillitis and bullous purpura to the upper and lower limbs. Six weeks prior to admission, she developed a sinus infection with rhinorrhea, congestion, bloody nasal discharge, productive cough, and bilateral hearing loss. Her hearing loss coincided with bilateral bloody and purulent drainage. She also experienced mild chest discomfort and shortness of breath, for which she was started on a 10-day course of Amoxicillin for presumed pneumonia. On day 8 of 10 she developed a rash and the medication was stopped. She reported experiencing a rash and facial swelling with Amoxicillin in the past but stated her current symptoms are different. She denied any personal or family history of autoimmune conditions. She denied polyarthralgia, abdominal pain, shortness of breath, or sinus complaints at the time of admission. Physical examination was significant for bilateral hearing loss (right sensorineural, left mixed), right-sided necrotizing tonsillitis, oral ulcers, and numerous tender, bullous lesions on bilateral upper and lower extremities.

Laboratory results showed a white blood cell count 10.360  $10^3/\mu\text{L}$  (reference range: 4.30-11.10  $10^3/\mu\text{L}$ ), hemoglobin 10.5 g/dL (reference range: 11.6-15.0 g/dL), platelet count 374  $10^3/\mu\text{L}$  (reference range: 116-358  $10^3/\mu\text{L}$ ). No eosinophilia is present, indicating a low likelihood of eosinophilic granulomatosis with polyangiitis. Ferritin 177.0 ng/mL (reference range: 6.0-137.0 ng/mL), C-reactive protein 23.4 mg/dL (reference range: <0.8 mg/dL), rheumatoid factor 531 IU/mL (reference range: <20 IU/mL). The laboratory values demonstrated an inflammatory response, possibly related to an autoimmune process. Therefore, we pursued an autoimmune and vasculitis workup. Myeloperoxidase antibodies IgG negative, <0.2 U/mL (reference range:  $\leq 3.5$  U/mL). Proteinase 3 antibodies IgG positive, 46.0 U/mL (reference range:  $\leq 2.0$  U/mL). Anti-proteinase 3 is highly specific for granulomatosis with polyangiitis. Anti-proteinase 3 positivity coupled with a negative anti-myeloperoxidase increased our suspicion for granulomatosis with polyangiitis.

Hepatitis C virus and mononucleosis serologies were negative. Antinuclear antibody screen was negative, excluding vasculitis mimics such as Sjögren's syndrome and rheumatoid arthritis. Urinalysis positive for blood (2+), otherwise unremarkable. eGFR and creatinine were within normal limits, thus decreasing concern for extensive kidney involvement seen in some cases of granulomatosis with polyangiitis. The skin biopsy

showed evidence of leukocytoclastic vasculitis of the superficial dermal capillary plexus with marked fibrinoid vascular necrosis. Although leukocytoclastic vasculitis is typically nonspecific, IgG, IgA, IgM, and C3 deposition were present, findings consistent with granulomatosis with polyangiitis. A chest x-ray assessing for lung involvement was negative. An MRI brain was done to evaluate the patient's hearing loss. A normal symmetric appearance of the internal auditory canals without mastoiditis was noted and cerebellopontine angle mass lesions were not observed (Figure 1).



**Figure 1:** Diffuse bullous purpuric rash throughout bilateral lower extremities. Bilateral upper extremities and trunk involvement were also present.

Early in the hospital course, IgA vasculitis was the team's primary concern due to the patient's recent amoxicillin exposure and extensive bullous purpura on physical examination. However, the presence of serum anti-proteinase 3 with the lack of IgA dominance on skin biopsy, coupled with an absence of abdominal pain and polyarthralgia strongly suggested that IgA vasculitis was unlikely.

Considering the patient's history of nasal involvement, hearing loss, and anti-proteinase 3 positivity, granulomatosis with polyangiitis was diagnosed in accordance with the American College of Rheumatology criteria despite atypical findings of bullous purpura [4]. The patient was started on induction therapy which included a single high dose of IV Methylprednisolone (500 mg) followed by oral Prednisone daily (60 mg), and Rituximab infusions four times weekly. The patient was also placed on Trimethoprim/sulfamethoxazole (800 mg/160 mg) administered Monday, Wednesday, and Friday for pneumocystis pneumonia prophylaxis. After attainment of stable remission with induction therapy, the maintenance regimen will consist of Rituximab for 12-24 months [5].

## Discussion

The clinical presentations of granulomatosis with polyangiitis and other vasculitis syndromes are widely variable, therefore reaching a diagnosis can be an arduous process. Diagnostic evaluation is imperative for distinguishing granulomatosis with polyangiitis from other causes of vasculitis includes anti-neutrophil cytoplasmic antibodies (ANCA). Importantly, cytoplasmic anti-neutrophil cytoplasmic antibodies (c-ANCA) against proteinase 3 are present in 80-90% of granulomatosis with polyangiitis cases with the remaining 10-20% of cases demonstrating perinuclear anti-neutrophil cytoplasmic antibodies (p-ANCA) against myeloperoxidase negativity [1].

Six reported cases demonstrate instances of granulomatosis with polyangiitis presenting similarly to IgA vasculitis, resulting in the misdiagnosis of pediatric patients [6-11]. Such occurrences are less prevalent in the adult population due to the lower frequency of IgA vasculitis in this demographic. Similar to granulomatosis with polyangiitis, IgA vasculitis presents with cutaneous eruptions and kidney involvement. Dermatological involvement is often the catalyst for clinical workup. IgA vasculitis typically presents with a bullous rash, while granulomatosis with polyangiitis often manifests with palpable purpura. This case demonstrates that the presence of a bullous rash does not exclude a possible diagnosis of granulomatosis with polyangiitis. Granulomatosis with polyangiitis is treated with immunosuppressive agents, [1] while IgA vasculitis is typically self-limiting and managed supportively. Due to the differences in management, mistaking granulomatosis with polyangiitis for IgA vasculitis leads to inadequate treatment of the underlying pathology.

The incarcerated status of our patient complicated her case, as inmates typically face delays in medical care, resulting in significant disease progression. Upon admission, her symptoms typical of granulomatosis with polyangiitis (sinusitis, nasal congestion, cough) had resolved, further reducing diagnostic clarity. Our case report emphasizes similarities in clinical presentation of IgA vasculitis and granulomatosis with polyangiitis while underscoring the diverse range of symptoms observed throughout disease progression. We highlight the importance of timely workup with biopsy and anti-proteinase 3 positivity screening as early diagnosis can prevent long-term complications.

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**Ethics Approval Statement:** Our institution does not require ethics approval for reporting individual cases or case series.

**Patient Consent Statement:** Written informed consent was obtained for anonymized patient information to be published in this article.

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